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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/470,489	06/06/95	MONTAGNIER	2506.0011-09

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EXAMINER	
PARKIN,J	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

See the attached.

Office Action Summary	Application No. 08/470,489	Applicant(s) Montagnier et al.
	Examiner Jeffrey S. Parkin, Ph.D.	Group Art Unit 1813

☒ Responsive to communication(s) filed on *3 Jul 1997* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *42-49, 52-59, and 62-71* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *42-49, 52-59, and 62-71* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Response to 37 C.F.R. § 1.129(a) Amendment

Status of the Claims

1. Since this application is eligible for the transitional procedure of 37 C.F.R. § 1.129(a), and the fee set forth in 37 C.F.R. § 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 C.F.R. § 1.129(a). Applicants' submission after final filed on January 09, 1997, has been entered. Claims 42-49, 52-59, and 62-70 were amended. Claims 42-49, 52-59, and 62-71 are pending in the application.

Petition to Correct Inventorship Pursuant to 37 C.F.R. § 1.48

2. In view of the papers filed August 08, 1997, it has been found that this non-provisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 C.F.R. § 1.48(b). The inventorship of this application has been amended by deletion of the following names: Solange Chamaret, Marianne Rey, Christine Rouzioux, and Christine Katlama.

35 U.S.C. § 112, First Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 42-49, 52-59, and 62-71 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The amended claim language is directed toward HIV-2 nucleic acid **probes that do not hybridize to nucleotides 2170-2240 and 5290-9130 of HIV-1.** Applicants' response fails to identify those regions of the specification that provide direct support for the specific claim limitations. Amendment of the claim language to exclude this limitation would obviate the rejection.

5. Claims 42-49, 52-59, and 62-71 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Claims 42-49 are directed toward methods for the detection of HIV-2 RNA employing nucleic acid probes complementary to HIV-2 nucleic acids which are selected from the group consisting of nucleic acids that do not hybridize to nucleotides 5290-9130 or 2170-2240 of HIV-1 under "non-stringent" conditions. Claims 52-59 are directed toward methods for the production of HIV-2 hybridization probes as described *supra*. Claims 62-71 are drawn toward methods for the detection of HIV-2 nucleic acids employing the aforementioned probes. The disclosure provides the complete nucleotide sequence of a clone corresponding to nucleotides 1-380 of the U3/R region of the HIV-2 proviral genome (refer to Figure 6). Upon review of the disclosure the skilled artisan would be capable of employing this full-length sub-genomic viral fragment as a probe for the detection of HIV-2. Applicants may obviate the enablement rejection by directing the claim language toward this specific probe (i.e., . . . wherein said probe consists of the following nucleotide sequence: 5'-GTGGA . . . AAGCA-3'.).

However, the broadly recited claim language is presently directed toward any probe comprising a "nucleic acid complementary to HIV-2 nucleic acid, and wherein said nucleic acid is selected from the group consisting of nucleic acid that does not hybridize to nucleotides 5290-9130 of HIV-1 under non-stringent conditions and nucleic acid that does not hybridize to nucleotides 2170-2240 of HIV-1 under non-stringent conditions . . . ." Applicants submit that they need not teach the corresponding genomic locations, nucleotide sequences, lengths, and specificity of all probes that function in the claimed method. Applicants further suggest that the hybridization conditions are well-known in the art and sufficiently defined in the disclosure. Finally, applicants argue that one skilled in the art could generate a cDNA corresponding to the full-length genomic RNA. Applicants' arguments have been thoroughly considered but are not deemed persuasive for the reasons of record in Paper nos. 5, 9, and 16, and as further enumerated below.

As previously set forth, the broadly recited claim language is directed toward any probe that **"comprises nucleic acid complementary to HIV-2 RNA"**. However, the disclosure does not provide any guidance pertaining to the selection of probes that would function in the recited method. The claim language encompasses full-length genomic sequences, sub-genomic fragments, and oligonucleotides of varying lengths. The ability to detect HIV-2 RNA will be contingent upon the precise sequence selected and the source of the nucleic acid. According to the present claim language, any nucleic acid (i.e., cellular or viral) that hybridizes with HIV-2 RNA would be encompassed. However, the specification fails to teach the corresponding genomic locations (i.e., LTR, *gag*, *pol*, *env*, etc.), precise nucleotide sequences, lengths, and specificity of said probes that would function in the recited assay.

Moreover, legal precedence dictates that the scope of the claims must bear a reasonable correlation to the scope of enablement

provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C. 1991). The court in *In re Vaeck* stated that "It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). However, **there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility.**"

Further guidance pertaining to genus/species relationships was provided in *Fujikawa v. Wattanasin*, 39 U.S.P.Q.2d 1895 (C.A.F.C. 1996). The court decided that "**simply describing large genus of compounds is not sufficient to satisfy written description requirement as to particular species or sub-genus.**" It was further noted that the claimed sub-genus was not described *ipsis verbis* in the specification and their was no indication as to what compounds, other than those disclosed as preferred, might be of special interest. Furthermore, several courts have upheld the requirement that satisfaction of the written description pertaining to DNA molecules requires a "precise definition" of nucleic acid sequence to be employed. *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 U.S.P.Q.2d 1016 (C.A.F.C. 1991). *Fiers v. Sugano* 25 U.S.P.Q.2d 1601 (C.A.F.C. 1993). *In re Bell* 26 U.S.P.Q.2d 1529 (C.A.F.C. 1993). *In re Deuel* 34 U.S.P.Q.2d 1210 (C.A.F.C. 1995). *University of California v. Eli Lilly and Co.*, 39 U.S.P.Q.2d 1225 (D.C. S.Ind. 1995). *Fiers v. Revel*, 25 U.S.P.Q.2d 1601 (C.A.F.C. 1993). The court emphasized in *Fiers v. Revel* that a "Disclosure sufficient to

satisfy written description requirement of 35 U.S.C. § 112 for claimed DNA sequence must have same degree of specificity as disclosure which demonstrates conception, and **must therefore include precise definition of DNA, such as by structure, formula, chemical name, or physical properties** . . . ." Applicants have clearly not met their burden under the first paragraph pertaining to an adequate written description of those nucleotide probes that can reasonably be expected to function in the recited manner.

Furthermore, the specification does not provide any guidance pertaining to the selection of appropriate hybridization and washing conditions under which the purported probes would successfully detect HIV-2 nucleic acids (e.g., viral genomic RNA, viral mRNAs, or proviral genomic DNA). Applicants are reminded that limitations from the specification are not read into the claims. *In re Van Geuns*, 988 F.2d 1181, 26 U.S.P.Q.2d 1057 (Fed. Cir. 1993). *Constant v. Advance Micro-Devices, Inc.*, 848 F.2d 1560, 7 U.S.P.Q.2d 1057, 1064-1065 (Fed. Cir.), *cert. denied*, 488 U.S. 892 (1988). *Ex parte McCullough*, 7 U.S.P.Q.2d 1889, 1891 (Bd. Pat. App. & Inter. 1987). *D.M.I., Inc. v. Deere & Co.*, 755 F.2d 1570, 225 U.S.P.Q. 236 (Fed. Cir. 1985). The hybridization conditions and washing conditions are critical for hybridization studies. Said conditions will vary considerably depending upon the probe size, it's genomic location (i.e., LTR vs. *env*), G-C content, and the corresponding melting temperature (T_m). As previously disclosed, this aspect of the rejection may be obviated by clearly disclosing the hybridization and washing conditions (i.e., high stringency wash consisting of 0.1X SSC, 0.1% SDS at 65 degrees for 30 min. or low stringency wash consisting of 2X SSC, 0.1% SDS at 50 degrees for 30 min.) under which the claimed probes would function in the claimed methods.

Finally, the invention also encompasses cDNA probes that may be employed in the instantly claimed method. The term "cDNA" is defined in the art as a product consisting of a double-stranded DNA sequence

obtained by the *in vitro* enzymatic conversion (via reverse transcriptase) of mRNA into double-stranded DNA. However, **the specification only teaches the generation of one specific cDNA clone, pSPE2.** The remaining nucleic acids (pROD 27-5, pROD 35-3, pROD 4.6, pROD 4.8, and pROD 4.7) described in the specification were generated from **genomic DNA libraries** and **are not cDNA probes.** Nucleic acid sequences corresponding to other cDNAs are not taught in the specification. It is well known in the art that genomic viral RNAs contain considerable secondary structure that impedes the ability of reverse transcriptase to synthesize a corresponding cDNA. It seems quite improbable that the skilled artisan could generate a cDNA corresponding to the full-length viral genome, *gag*, *pol*, or *env*.

Finally, the legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments. The board disclosed these considerations in *Ex parte Forman* as follows:

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art: *Ansul Co. v. Uniroyal, Inc.*, supra. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965); *In re Colianni*, *supra*.

In the instant application the disclosure fails to provide adequate guidance concerning a number of these considerations as they pertain to the claimed invention. The specification only provides a very

limited number of working embodiments and fails to provide sufficient guidance pertaining to the identification and selection of those nucleic acids that will function in the desired manner. The disclosure also fails to provide adequate guidance pertaining to the appropriate hybridization parameters under which said probes will function correctly. The prior art fails to provide appropriate guidance pertaining to these various scientific parameters thereby contributing to the unpredictability associated with the claimed invention. Finally, the breadth of the claim language fails to receive appropriate support. When all of the aforementioned issues are considered *in toto*, it would clearly require undue experimentation the skilled artisan to ascertain all the scientific parameters required to practice the instantly claimed invention.

35 U.S.C. § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. The previous rejection of claims 42, 52, and 62 under 35 U.S.C. § 102(a) as being anticipated by Clavel *et al.* (1986), is hereby withdrawn in response to applicants' amendment.

8. The previous rejection of claims 42-44, 52-54, and 62-64 under 35 U.S.C. § 102(a) as being anticipated by Clavel *et al.* (1986), is hereby withdrawn in response to applicants' amendment.

Non-statutory Double Patenting

9. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 U.S.P.Q. 644 (C.C.P.A. 1969). *In re Vogel,* 422 F.2d 438, 164 U.S.P.Q. 619 (C.C.P.A. 1970). *In re Van Ornum,* 686 F.2d 937, 214 U.S.P.Q. 761 (C.C.P.A. 1982). *In re Longi,* 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985). *In re Goodman,* 29 U.S.P.Q.2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d).Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. § 3.73(b).

10. The *provisional* rejection of claims 42-49, 52-59, and 62-71 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42-46 and 48-50 of copending application Serial No. 08/392,613 is hereby withdrawn in response to applicants' amendment.

11. Claims 42, 49, 52, 59, 62, and 69 stand ***provisionally*** rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 83 of copending application Serial No. 08/250,103. The '103 application discloses an HIV-2_{ROD} cloned nucleic acid obtained from the *env* region of the viral genome. The nucleotide sequence disclosed is identical to the *env* sequence presented in the instant application (refer to pages 58-61

of the specification). This nucleic acid clearly "corresponds to HIV-2 RNA" and would be useful for the detection of HIV-2 in biological specimens. Accordingly, one of ordinary skill in the art would be motivated to utilize these nucleic acids in an *in vitro* diagnostic assay to identify HIV-2.

This is a **provisional** obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

35 U.S.C. § 112, Second Paragraph

12. The previous rejection of claims 42-49 and claims 62-69 under 35 U.S.C. § 112, second paragraph, as being multiplicative (refer to M.P.E.P. § 2173.05(n)), is hereby withdrawn in response to applicants' amendment.

Correspondence

13. Correspondence related to this application may be submitted to Group 1813 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). **Official communications should be directed toward one of the following Group 1800 fax numbers: (703) 308-4242 or (703) 305-3014.** Informal communications may be submitted directly to the Examiner through the following fax number: (703) 305-7939. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

14. Any inquiry concerning this communication should be directed to **Jeffrey S. Parkin, Ph.D.**, whose telephone number is **(703) 308-2227.** The examiner can normally be reached Monday through Friday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, **Donald E. Adams, Ph.D.**, can be reached at **(703) 308-0570.** Any inquiry of a general nature or relating to the

status of this application should be directed to the Group 1813 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1813

September 12, 1997